The Risks of Prostate Cancer Detection by Transrectal Ultrasound Guide Biopsy in Thai Men with Abnormal Prostatic-Specific Antigen or Abnormal Digital Rectal Examination

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Abstract

Objective : To determine the risks of prostate cancer detection in Thai men with abnormal prostatic-specific antigen (PSA) or abnormal digital rectal examination (DRE).

Material and Method : One hundred and forty four Thai men with abnormal PSA or abnormal DRE or both were biopsied at the prostate gland with the use of transrectal ultrasound guide biopsy (TRUSBX). The risks of prostate cancer detection were evaluated.

Results : Mean age was 65.7 years old (S.D. = 9.88). The risks of positive biopsy according to the PSA levels of 0-4 ng/ml, 4.1-10 ng/ml, 10.1-20 ng/ml, 20.1-50 ng/ml, 50.1-100 ng/ml and more than 100 ng/ml were 6.25 per cent, 6.67 per cent, 10.8 per cent, 33.3 per cent, 60 per cent and 100 per cent, respectively. The risks of positive biopsy according to DRE appearances of total hard consistency, nodule, induration and benign prostatic hyperplasia were 57.1 per cent, 23.5 per cent, 34.6 per cent and 10 per cent, respectively. Of 144 men, 32 had adenocarcinoma of prostate. Radical prostatectomy was performed on 15 patients with clinically localized disease. Ten patients (66.6%) had free margin on their pathological specimens and 6 (40%) had organ confined disease.

Conclusion : PSA testing alone or DRE alone is not a perfect test to diagnose prostate cancer since prostate cancer may present in men with normal PSA or men with no suspicious cancer DRE. For early detection of prostate cancer, both PSA testing and DRE need to be performed. When either PSA testing or DRE or both is abnormal, TRUSBX should be carried out.

Keyword : Prostate, Prostatic Carcinoma, Prostatic-Specific Antigen

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Today, the incidence of prostate cancer in Thailand has increased since prostatic-specific antigen (PSA) was utilized[1-3]. In the past, most prostate cancers were detected by transurethral resection prostatectomy (TUR-P) in patients with symptoms of prostatism or urinary retention[2]. Currently, transrectal ultrasound guide biopsy (TRUSBX) has been utilized in Siriraj Hospital to detect prostate cancer in men with abnormal PSA or abnormal digital rectal examination (DRE). Several reports showed the risks of prostate cancer detection in men with abnormal PSA or abnormal DRE in Western countries where incidences were higher[4-6]. To determine the risks of prostate cancer detection in Thai men with abnormal PSA or abnormal DRE by transrectal ultrasound guide biopsy, we conducted our protocol.

MATERIAL AND METHOD

From March 1999 to January 2000, 144 Thai men were registered to undergo a prostatic biopsy at the Division of Urology, Siriraj Hospital. The indications for prostatic biopsy were either abnormal PSA or abnormal DRE or both. Before the procedure, histories of lower tract symptoms were recorded. All patients were biopsied at their prostate with the use of transrectal ultrasound guide and a bioptic gun in the outpatient unit. All PSA tests used were the total PSA of Cobas Core Total EIA[7]. PSA levels of 0-4 ng/ml were defined as normal PSA. Other levels of more than 4 ng/ml were defined as abnormal PSA. All DRE were evaluated by the urologists in our division. DRE appearances in our series were classified as total hard consistency, nodule, induration and benign prostate hyperplasia (BPH). The three former implied suspicious prostate cancer and were defined as abnormal DRE. On the other hand, benign prostatic hyperplasia implied no suspicion of prostate cancer. The procedure used was six systemic sextants as described by Hodge et al[8]. In addition, if there were any nodules or hypoechoic lesions, these lesions were also biopsied. All patients had oral antibiotic prophylaxis before the procedure which was continuously administered for three days at home. All biopsied specimens were reviewed by one pathologist. All prostatic biopsy data in this analysis was the outcome of the first biopsy in each patient. The outcomes of the repeated biopsies were excluded from this study. The risks of positive biopsy were determined according to the PSA levels of 0-4 ng/ml, 4.1-10 ng/ml, 10.1-20 ng/ml, 20.1-50 ng/ml, 50.1-100 ng/ml and more than 100 ng/ml. The risks of positive biopsy were also evaluated according to the DRE appearances classified above. Statistical analysis was made with the use of SPSS program[9]. Chi-square test was used to calculate P value.

RESULTS

The patient's ages ranged from 18 to 89 years old. Only 4 men were biopsied at the age of less than 50 because they had symptoms of prostatism and their DRE appearances were suspicious of malignancy. Of 4 men, 2 had no malignancy, one had adenocarcinoma and the other had unspecified sarcoma. The majority of men were more than 60 years old with the mean age of 65.7 (S.D. = 9.88). Considering lower tract symptoms, 89.7 per cent and 6.3 per cent had prostatism and hematuria, respectively. All DRE were performed in 144 men but only 128 men had PSA testing. Of 144 men, 32 (22.2%) had adenocarcinoma, 3 (2.1%) had other malignancy and 109 (75.7%) had no malignancy. Regarding PSA testing only, Table 1 shows the risks of prostate cancer detection in 128 men with various PSA levels. The higher the PSA levels, the higher the risk of prostate cancer detection which was shown with statistically significant difference (P value < 0.0001). Significantly, all men with PSA levels of more than 100 ng/ml had adenocarcinoma of the prostate. Regarding DRE appearances only, Table 2 shows the risks of prostate cancer detection on various DRE appearances. Men with suspicious cancer DRE showed higher risks of adenocarcinoma of the prostate when compared to those with no suspicious cancer DRE with statistically significant difference (P value < 0.01). Regarding both PSA testing and DRE, the risks of adenocarcinoma of prostate are shown in Table 3 and Table 4. In each range of abnormal PSA levels of 0–100 ng/ml, the risks of prostate cancer were higher when those men had an abnormal DRE. As shown in Table 4, the risks of prostate cancer detection in men with both abnormal PSA levels of 4.1-50 ng/ml and abnormal DRE were higher when compared to men with abnormal DRE alone or men with abnormal PSA levels of 4.1-50 ng/ml alone.

Table 1. The risks of prostate cancer detection in Thai men with abnormal PSA levels.

PSA levels (ng/ml)	No. of men with malignancy				
	No.	Adenocarcinoma	%	Other malignancy	%
0-4	16	1	6.25	0	0
4.1-10	45	3	6.67	0	0
10.1-20	37	4	10.8	0	0
20.1-50	18	6	33.3	1	5.6
50.1-100	5	3	60	0	0
> 100	7	7	100	0	0

Table 2. The risks of prostate cancer detection in Thai men with abnormal DRE appearances.

DRE appearances	No. of men with malignancy				
	No.	Adenocarcinoma	%	Other malignancy	%
Total hard consistency	14	8	57.1	0	0
Nodule	34	8	23.5	0	0
Induration	26	9	34.6	2	7.7
BPH	70	7	10	1	1.4

Table 3. The risks of adenocarcinoma of prostate in Thai men with abnormal testing.

PSA levels ng/ml	DRE appearances					
	No suspicious cancer			Suspicious cancer		
	No. of patients	Adenocarcinoma	%	No. of patients	Adenocarcinoma	%
0-4	2	0	0	14	1	7.1
4.1-10	30	1	3.3	15	2	13.3
10.1-20	26	0	0	11	4	36.3
20.1-50	8	3	37.5	10	3	30
50.1-100	1	0	0	4	3	75

Table 4. The risks of adenocarcinoma of prostate in Thai men with either abnormal PSA levels of 4.1-50 ng/ml alone or abnormal DRE alone or both.

Test results	No. patients	Adenocarcinoma	%
PSA 0-4 ng/ml, abnormal DRE	14	1	7.1
PSA 4.1-50 ng/ml, no suspicious cancer DRE	64	4	6.3
PSA 4.1-50 ng/ml, abnormal DRE	36	9	24.3

Of 32 patients with adenocarcinoma of prostate, 10 patients with PSA levels of more than 50 ng/ml had their staging beyond localized disease. Of 22 patients with PSA levels of 50 ng/ml or less, 15 (68.2%) were classified as clinically localized disease and underwent radical prostatectomy. Another 7 (31.8%) patients were treated with other forms of therapies because their prostate cancer staging was beyond localized disease or they were too old. Of 15 patients with radical prostatectomy, all had no lymph node metastasis. Ten patients (66.6%) had free margin

on their pathological specimens. Six (40%) had organ confined disease.

Complications of TRUSBX were hematuria or bleeding per rectum but these were minor complications. They were spontaneously resolved within 48-72 hours. We had 2 cases of major complications that needed hospitalization. One had blood clot retention in the bladder and the other had septicemia and needed parenteral antibiotic. However, this patient did not administer the prophylactic antibiotic adequately. There was no mortality in our series.

DISCUSSION

The objective of this study was to determine the risks of prostate cancer detection in Thai men with abnormal PSA testing or abnormal DRE. As shown in Table 1, the higher the PSA level, the higher the risk of prostate cancer. This agrees with reports from Western countries[4-6]. However, compared to the risks of prostate cancer in the Western countries, the risks of prostate cancer detection in Thai men with abnormal testing are lower. This may be the reason why the incidence of prostate cancer in Thailand is lower than that of Western countries[2]. To our knowledge, the risks of prostate cancer detection with the use of TRUSBX in Thai men have never been reported in the literature. Thus, we advocate using our data for physicians and patients to discuss the chance of prostate cancer detection when an abnormal PSA testing or an abnormal DRE is discovered. For PSA levels of 4.1-20 ng/ml, the risks of prostate cancer detection are between 7 per cent and 10 per cent. For PSA levels of 20.1-50 ng/ml, the risk increases to 33 per cent. When the PSA level is higher than 50 ng/ml, 60 per cent of men would have prostate cancer. Significantly, all men have prostate cancer if their PSA level is above 100 ng/ml. However, one thing should be considered, all PSA testing used in this study was one assay only. Thus, our data has no bias of variation among the assays used. When considering data of other PSA assays, it needs to be correlated with this assay because different assays may show different PSA levels[3,10]. DRE is another test for prostate cancer detection. When DRE appearance is suspicious of cancer, the risk of prostate cancer is higher than DRE with no suspicious cancer. If DRE appearance shows nodule or induration, the risk of prostate cancer detection is approximately 30 per cent. When DRE appearance shows total hard consistency, the risk increases to nearly 60 per cent. Even although PSA and DRE are important tests for prostate cancer, they are not perfect. The reason is that 6.25 per cent of the patients with normal PSA testing had prostate cancer as shown in Table 1. These patients were biopsied because of abnormal DRE. On the other hand, DRE alone may miss diagnosis prostate cancer since 10 per cent of men with no suspicious cancer DRE appearance or BPH had prostate cancer as shown in Table 2. These men were biopsied because of abnormal PSA. As shown in Table 3 and Table 4, the risks of prostate cancer detection were highest when men had both abnormal PSA and abnormal DRE. Thus, we recommend that detection of prostate cancer needs both PSA testing and DRE. Our data agrees with other series[4-6].

It is well known that localized prostate cancer has an excellent survival rate while metastatic prostate cancer has a poor prognosis [2,11,12]. Since localized prostate cancer has no symptom, early detection should be utilized from PSA testing and DRE. When PSA testing or DRE is abnormal, TRUSBX should be carried out. Among our patients with adenocarcinoma of the prostate that were detected by TRUSBX in this series, we could detect more patients with clinically localized disease and treated them with radical prostatectomy. It was 68.2 per cent compared to almost 9 per cent in our previous series[2]. Importantly, of 32 newly diagnosed prostate cancer in this series, 18.8 per cent (6 from 32) were of pathological organ confined disease and 31.3 per cent (10 in 32) patients had free margin on their surgical specimens. Obviously, more localized prostate cancer patients were detected.

Nevertheless, the issue of when men with abnormal PSA should be biopsied is still controversial. Some urologists do not prefer performing a prostatic biopsy if the PSA level is not high enough. At present, the cutoff abnormal PSA level at which patients should undergo a prostatic biopsy has not yet been determined particularly in Thai men. The abnormal level of 4 ng/ml using in Western countries may not be appropriate for Thai men. Even though our data shows the risks of prostate cancer in various PSA levels, it can not precisely indicate where the cutoff abnormal

PSA level in Thai men is. Thus, further studies need to be conducted for determining the normal value of PSA in Thai men.

TRUSBX is a safe procedure. Most complications were minor and resolved spontaneously. If the appropriate antibiotic is applied, serious complications should not occur. In addition, no mortality was presented. At present, we believe that TRUSBX is the best method to detect prostate cancer early. Finally, this may help urologists detect more localized prostate cancer and may prolong survival with definitive treatment such as radical prostatectomy in an individual patient.

SAMMARY

PSA testing alone or DRE alone is not a perfect test to diagnose prostate cancer because prostate cancer may present in men with normal PSA or men with no suspicious cancer DRE. For early detection of prostate cancer, both PSA testing and DRE need to be performed. When either PSA testing or DRE or both is abnormal, TRUSBX should be carried out. The higher the PSA level, the higher the risk of prostate cancer. DRE with suspicious cancer has higher risks of prostate cancer than DRE with no suspicious cancer. TRUSBX yields greater localized prostate cancer detection. Even though our data shows the risks of prostate cancer detection in various PSA levels, the cutoff for abnormal PSA level has not yet been determined in Thai men. Further studies to indicate the normal PSA level in Thai men need to be conducted.

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อัตราเสี่ยงของมะเร็งต่อมลูกหมากในการตัดเนื้อตรวจโดยการใช้อัลตร้าซาวด์นำทางในชายไทยที่มีค่าพรอสตาติก-สเปคซิฟิก แอนติเจน หรือการตรวจต่อมลูกหมากที่ผิดปกติโดยนิ้วทางทวารหนัก

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วัตถุประสงค์ : เพื่อต้องการหาอัตราเสี่ยงของการค้นพบมะเร็งต่อมลูกหมากในชายไทยที่มีค่าพรอสตาติก-สเปคซิฟิก แอนติเจน (PSA) ที่ผิดปกติ หรือการตรวจต่อมลูกหมากโดยนิ้วทางทวารหนัก (DRE) ที่ผิดปกติ

ผู้ป่วยและวิธีการ : ชายไทย 144 คน ที่มีความผิดปกติของค่า PSA หรือ DRE ได้ทำการตัดเนื้อตรวจเพื่อหามะเร็งต่อมลูกหมากโดยการใช้อัลตร้าซาวด์นำทาง (TRUSBX) ผลของการตัดเนื้อตรวจได้นำมาวิเคราะห์

ผล : อายุเฉลี่ยของชายไทยกลุ่มนี้เท่ากับ 65.7 ปี โอกาสที่ชายไทยเป็นมะเร็งต่อมลูกหมากจำแนกตามค่า PSA ได้ดังนี้ ระดับ PSA 0-4 ng/ml, 4.1-10 ng/ml, 10.1-10 ng/ml, 20.1-50 ng/ml, 50.1-100 ng/ml และ มากกว่า 100 ng/ml โอกาสคือ 6.25%, 6.67%, 10.8%, 33.3%, 60% และ 100% ตามลำดับ โอกาสที่ชายไทยเป็นมะเร็งต่อมลูกหมากจำแนกตาม DRE ได้ดังนี้ ต่อมลูกหมากแข็งทั้งต่อม, ต่อมลูกหมากคลำได้เป็นตุ่ม, ต่อมลูกหมากคลำได้แข็งบางส่วน, ต่อมลูกหมากโตธรรมดา โอกาสคือ 57.1, 23.5%, 34.6% และ 10% ตามลำดับ ในชาย 144 คนพบว่า 32 คน เป็นมะเร็งต่อมลูกหมาก ในผู้ป่วย 15 คน ที่ได้รับการผ่าตัด radical prostatectomy พบว่า 66.6% ของผู้ป่วยสามารถเอาก้อนทูมออกได้หมด และ 40% ของผู้ป่วยมะเร็งต่อมลูกหมากไม่กระจายออกนอกต่อมลูกหมาก

สรุป : การตรวจ PSA อย่างเดียวหรือ DRE อย่างเดียวไม่เพียงพอที่จะให้การวินิจฉัยมะเร็งต่อมลูกหมากได้สมบูรณ์ เนื่องจากมะเร็งต่อมลูกหมากสามารถพบได้ในชายไทยที่มีค่า PSA ปกติ หรือการตรวจ DRE ที่ปกติได้ ดังนั้นเพื่อจะวินิจฉัยมะเร็งต่อมลูกหมากให้ได้ในระยะต้น การตรวจทั้ง PSA และ DRE มีตามจำเป็นต้องทำ ถ้าการตรวจ PSA หรือ DRE มีความผิดปกติ ชายไทยผู้นั้นควรจะได้รับการทำ TRUSBX

คำสำคัญ : ต่อมลูกหมาก, มะเร็งต่อมลูกหมาก, พรอสตาติก-สเปคซิฟิก แอนติเจน

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